IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
10/736,084	12/15/2003	Joseph C. Walsh	2003P88073US

Response To **OFFICIAL ACTION**

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REMARKS

Claims 1-32 are pending in the present application. Claims 33-34 were cancelled in the response of May 31, 2006. Claims 1, 10,11, 12, 21, and 30 have been amended in the present response.

On page 2 of the Office Action, the Examiner requested a new title indicative of the invention to which the pending claims are directed.

Accordingly, Applicants have amended the title as noted above.

Claims Objections

The Examiner objected to Claims 1, 21, 29 and 30 because the claims "recite structures that are not big enough to see all the substitution and atoms clearly." The structures of Claim 1, 21, 29 and 30 have been enlarged to improve clarity. Withdrawal of the rejection to these Claims is respectfully requested.

The Examiner objected to Claim 12, requesting that the notation FLT should be expanded at the first occurrence. Applicants have expanded the notation FLT as requested. Withdrawal of the rejection to Claim 12 is respectfully requested.

Claim Rejections- 35 USC § 112

The Examiner rejected Claims 10-11 and 30-32 under 35 U.S.C. § 112, first paragraph, allegedly because the specification, while being enabling for making the nucleoside as claimed where the base is thymidine and uridine, does not reasonably provide enablement for making the nucleoside wherein the base is other than thymidine or uridine. The Examiner quoted the factors of In re Wands and conclude that "the specification, at the time the application was filed, would not have taught one skilled in the art to make and/or use the full scope of the claimed invention without undue experimentation.

As amended, Claim 10 recite the method for preparing a precursor for the preparation of a radiolabled nucleoside "wherein the nucleoside base is thymidine or uridine." Similarly, Claim 11 has been amended to recite that the nucleoside base is also thymidine or uridine. Withdrawal of the 35 U.S.C. § 112, first paragraph rejection of Claims 10 and 11 is respectfully requested.

Independent Claim 30 explicitly recite a nucleoside wherein the structure of the compound is an enolate derivative of a thymidine nucleoside. In contrast to the Examiner's contention, Claim 30, and it's dependent Claims 31 and 32 do not recite a structure that is any other than a thymidine nucleoside. The Examples and Figures 1-3, for example, provided in the specification clearly teach the compounds that are clearly a nucleoside comprising a thymidine base.

Accordingly, Applicant respectfully assert that the teaching in the specification fully enable the full scope of the compounds recited in Claim 30 and it's dependent Claims 31 and 32. Withdrawal of the 35 U.S.C. § 112, first paragraph of Claims 30, 31 and 32 is respectfully requested.

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On page 6 of the Office Action, the Examiner rejected Claims 1-28 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

According to the Examiner, Claim 1 does not end in a period. As amended, Applicants have added a period in the last chemical structure of Claim 1. Withdrawal of the rejection is respectfully requested.

Claim 12 was rejected because the Examiner indicated that the notation "FLT" is not clear. As amended, the notation "FLT" has been expanded with the notation in amended and placed in parentheses. Withdrawal of the rejection is respectfully requested.

On page 6 of the Office Action, the Examiner rejected Claims 4, 12 and 21 because of the recitation that "R is C1-C4 alkyl, and the claims also recite i-propyl", which is the narrower species within the subgenus of C1-C4 alkyl. The group "i-propyl" has been deleted in Claims 4, 14, 21 and 30. There is no such "i-propyl" group in Claim 12. Withdrawal of the rejection of Claims 4, and 21, and as it may apply to presently amended Claims 14 and 30, is respectfully requested.

According to the Examiner, Claim 10 recites the broad recitation nucleoside, and the claim also recites pyrimidine, which is the narrower statement of the range/limitation. Applicants respectfully traverse the Examiner's characterization of these terms and rejection of Claim 10 in view of the Examiner's mis-characterization of Claim 10.

As it is well known in the art, the term nucleosides means any of various compounds consisting of a sugar, usually a ribose or a deoxyribose that is bonded to a base, such as a purine or pyrimidine base. These compounds may be obtained by hydrolysis of a nucleic acid, such as adenosine or guanine. Examples of such nucleosides include, adenosine, uridine, guanosine, cytidine, thymidine, etc ... Accordingly, a nucleoside may comprise of a base such as a pyrimidine Therefore, the term pyrimidine is not a narrower range or limitation of the term nucleoside, but it is a base component of a nucleoside. Withdrawal of the rejection of Claim 10 is respectfully requested.

Claim Rejections- 35 USC § 103

On page 7 of the Office Action, the Examiner rejected Claims 21-32 under 35 U.S.C. 103(a) as being unpatentable over Acevedo et al (US 6,060,592).

The Examiner then summarizes the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966) as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

On page 8 of the Office Action, the Examiner notes that

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"Acevedo et al teach pyrimidine nucleosides, thymidine, in particular (col. 8, lines 20-50; col. 9, lines 5-35), wherein a variety of substitutions are present at the 5'oxygen (protecting groups) and leaving groups including mesylate (col. 7, lines 7-30). It would have been obvious to one of ordinary skill in the art at the time the invention was made to make compounds as instantly claimed since the pyrimidine nucleosides with the structural features as instantly claimed are seen to be taught in the prior art. (Emphasis added)

One of ordinary skill in the art would be motivated to make the compounds as instantly claimed because of the presence of enol structure in the pyrimidine ring can be used in place of normal nucleotides to alter the properties, which can result in selective binding (col. 10, lines 41-65)."

For a chemical compound, a prima facie case of obviousness requires 'structural similarity between claimed and prior art subject matter ... where the prior art gives reason or motivation to make the claimed compositions.'" *In re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990) *(en banc);* accord, *In re Papesch*, 315 F.2d 381,391 (C. C. P. A. 1963). To prevent the distortions of hindsight from invalidating genuine inventions, close attention to the supposed reason or motivation for making the claimed compound is critical. As a leading treatise explains: Because of the unpredictable nature of chemical reactions, a newly-synthesized compound may be very similar in structure to known and existing compounds and yet exhibit very different properties. Further, many such new compounds are obvious in the sense that any competent chemist could have synthesized them *if requested or motivated to do so.* 2 Donald S. Chisum, Chisum on Patents §5.04[6] at 5-429 (2000) (emphasis added).

To show obviousness, the reason or motivation offered by the prior art need not offer "absolute predictability" of the results, but it requires at least a "reasonable expectation of success." *Yamanouchi*, 231 F.3d at 1343, quoting *In re Longi*, 759 F.2d 887, 896 (Fed. Cir. 1985); accord, *In re Vaeck*, 947 F.2d 488, 495 (Fed. Cir. 1991) (reversing PTO rejection of claims as obvious where prior art offered no "reasonable expectation of success"), citing *In re O'Farrell*, 853 F.2d 894, 903-04 (Fed. Cir. 1988).

If the prior art makes a particular experiment or modification only "obvious to try," that does not support a finding of obviousness. See *In re Eli Lilly and Co.*, 902 F.2d 943, 945 (Fed. Cir. 1990), citing *In re O'Farrell*, 853 F.2d at 903.

However, rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. In re Lee, 277 F.3d 1338 (Fed. Cir. 2002) at 1343-46, and In re Rouffet, 149 F.3d 1350 (Fed. Cir. 1998) at 1355-59.

Applicants respectfully assert that, notwithstanding the factual inquiries that may be used to determine whether the claimed invention is obvious in view of cited art, the disclosure or teaching of Acevedo et al neither makes obvious the presently claimed invention, nor do the teaching of Acevedo et al even suggest the subject matter that is even remotely related to the present invention.

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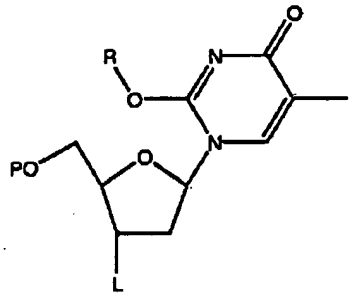
The Claimed Invention:

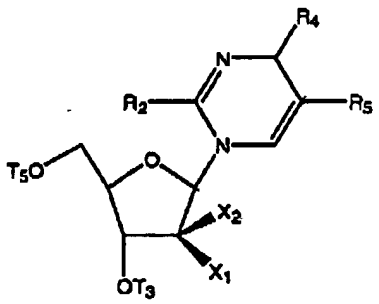
As noted above, the Examiner compared the structures of the claimed compounds recited in Claims 21-32 with the compounds disclosed by Acevedo et al, and concludes that "the pyrimidine nucleosides with the structural features as instantly claimed are seen to be taught in the prior art." Applicants respectfully disagree with the Examiner's conclusion.

First, Applicants note that, unlike one of the aspects of the present invention in which the compounds are prepared as ^{18}F-FLT or ^{18}F-FLT precursors for diagnostic imaging, such as by PET, for example (see paragraph [0001] and [0008]), the compounds of Acevedo et al are structurally different and are designed to be used for incorporation into oligonucleotides (column 1, lines 15-17) that may be useful as diagnostic reagents and research reagents.

Second, Applicants note that, as the Examiner also suggested, the compounds of Acevedo et al as shown in column 8 (shown in their various resonance-tautomeric forms), are significantly different from the compounds recited in Claim 21. In particular, as clearly shown below, while Acevedo et al discloses various pyrimidine nucleosides, **none of the compounds disclosed by Acevedo et al have the structures recited in Claim 21**.



Compound of Claim 21



Isomer of Acevedo et al (Column 8)

As noted above, because the compounds disclosed by Acevedo et al are designed to be used for incorporation into oligonucleotides, the substitution at the 3' position (i.e. the $-OT_3$ group) are specifically designed as "H, phosphate, an activated phosphate, a hydroxyl protecting group, a nucleoside, a nucleotide, an oligonucleotide or an oligonucleoside." See middle structure in column 8 and definition for T_3 in column 6, lines 43-45. On the other hand, the compounds recited in Claim 21 (and its dependent claims) of the present application have, at the 3' position, the group "L" that comprises a leaving group. Examples of such leaving groups are explicitly recited in Claim 27 and Claim 31. Applicants note that none of the leaving groups recited in Claims 27 and Claim 31 are structurally or functionally similar to the $-OT_3$ group of Acevedo et al. The $-OT_3$ group of Acevedo et al. are "H, phosphate, an activated phosphate, a hydroxyl protecting group, a nucleoside, a nucleotide, an oligonucleotide or an oligonucleoside", none of which are specifically defined by Acevedo et al. as constituting a "leaving group." See column 7, lines 18-30.

In addition, Acevedo et al specifically teach that the groups R_2 and R_4 (as defined by Q) on the pyrimidine base may be leaving groups. See column 3, lines 49 (R_2 and R_4 is Q), columns 3, lines 54 and 64 (Q is a leaving group); column 6, line 21, and line 26 and line 36. In

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contrast, as noted above, Claim 21 (and its dependent claims) of the present application teaches that the leaving group "L" must be on the ribose, not on the pyrimidine base. Accordingly, it is readily apparent from the disclosure of Acevedo et al that the disclosure teaches away from the compounds claimed in the present application because the compounds with the structures and functions of Acevedo et al are clearly distinct from the compounds claimed in the present application. Furthermore, Acevedo et al do not suggest, teach or motivate one skilled in the art to prepare or design the compounds recited and claimed in the present application.

On page 8 of the Office Action, the Examiner also asserts that "one of ordinary skill in the art would be motivated to make the compounds as instantly claimed because of the presence of enol structure in the pyrimidine ring can be used in place of normal nucleotides to alter the properties, which can result in selective binding." However, as the Federal Circuit has stated, if the prior art makes a particular experiment or modification only "obvious to try," that does not support a finding of obviousness, and mere conclusory statements instead of an articulated reasoning without some rational underpinning to support the legal conclusion of obviousness cannot support the examiner's contention that the claims of the present application is obvious in view of Acevedo et al.

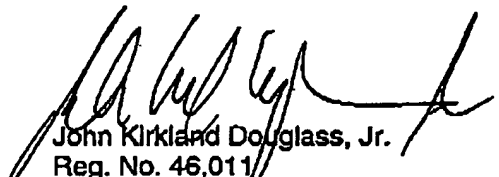
Applicants respectfully assert that the Examiner has not provided any proof of some teaching, suggestion or motivation to either suggest the intermediates, products nor processes for preparing the intermediates and products as claimed in the present application. Acevedo et al clearly and distinctly teach nucleoside compounds that are both structurally and functionally distinct from the compounds claimed in the present application.

Applicants respectfully request the withdrawal of the rejection of Claims 21-32 under 35 U.S.C. 103(a) rejection over Acevedo et al.

In view of the foregoing amendments and remarks, Applicant submits that all of the claims are in proper format and are patentably distinct from the prior art of record and are in condition for allowance.

The Examiner is invited to contact the undersigned at the telephone number listed below with any questions concerning this application.

Respectfully submitted,



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